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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/699,716	08/27/96	HEATH D	003/029/SAF

HM12/0201

US ARMY MEDICAL RESEARCH &
MATERIAL COMMAND
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EXAMINER	
DUFFY, P	
ART UNIT	**PAPER NUMBER**
1645	17

DATE MAILED: 02/01/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/699,716	Heath
Examiner	**Group Art Unit**
Duffy	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 4-13-98 + 2-25-99.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-3, 4-32 is/are pending in the application.

Of the above claim(s) 18-29 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-3, 4-17 + 30-32 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-3 ǂ 4-32 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

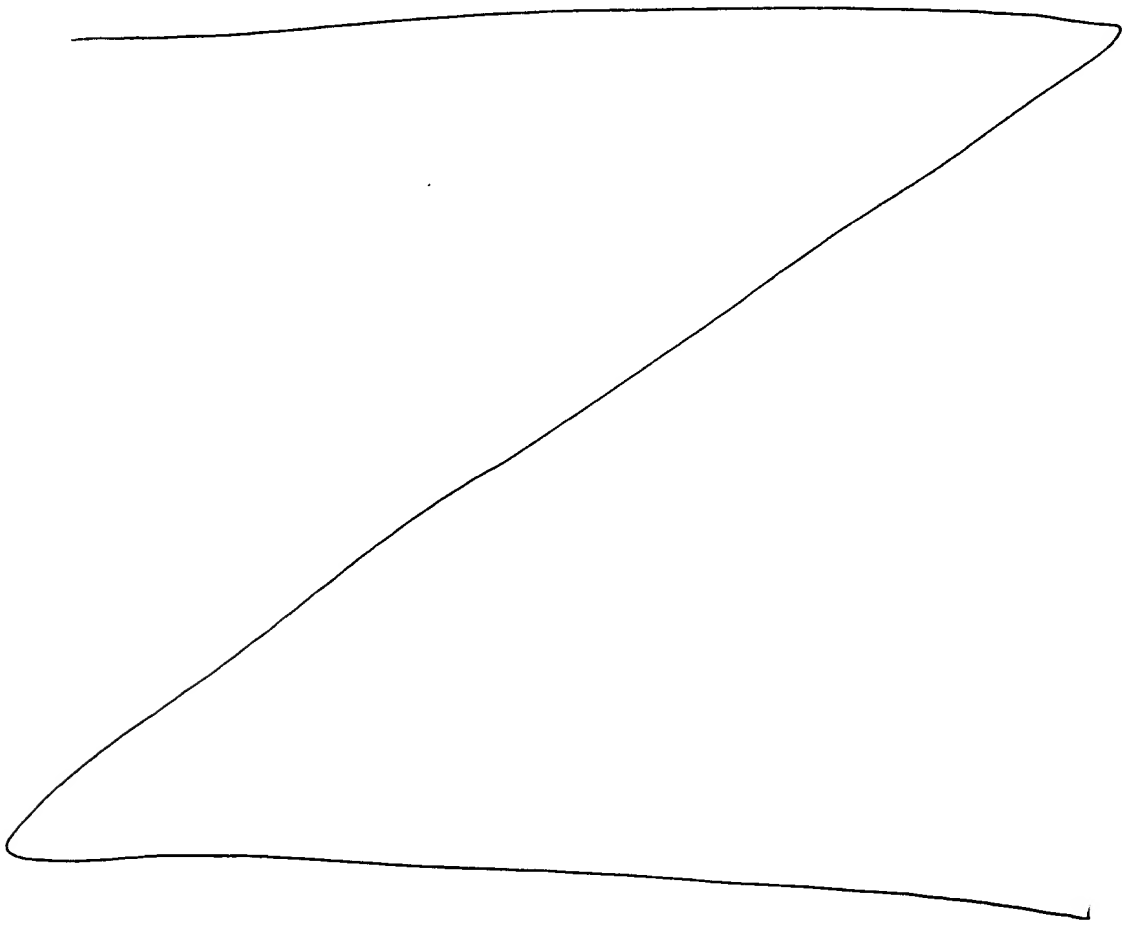
DETAILED ACTION

1. The amendment and responses filed 4-13-98 and 2-25-99 have been entered into the record. Claims 1-3, 5-17 and 30-32 are under examination.

2. Claim 18-29 are have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention(s). Election was made **without** traverse in Paper No. 7.

Rejections Withdrawn

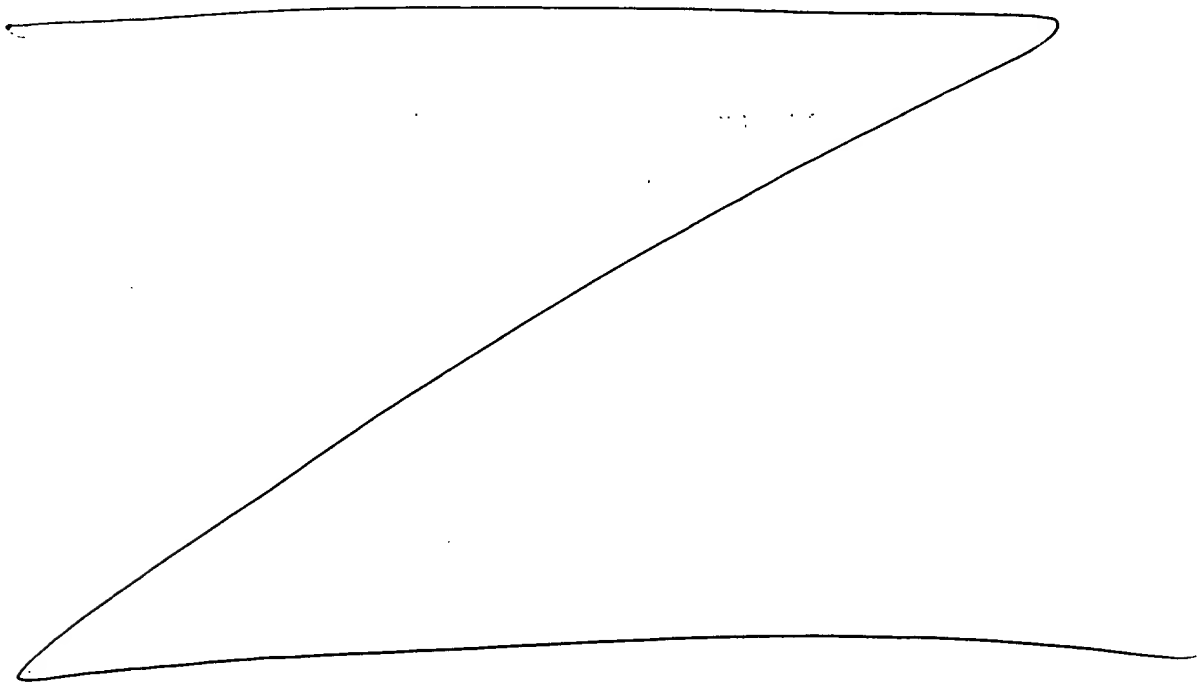
3. The rejection of claims 1-3 and 5-6 under 35 U.S.C. 102(b) as being anticipated by Price et al. (J. Bacteriology 171(10):5646-53 10/89) is withdrawn based on applicants amendment.



Objections to the Specification

4. The amendment filed 8-11-97 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment to correct the strain to recite "..the Antigua strain of *Y. pestis*..." at page 16, line 1. The specification does not apparently mention the use of the Antigua strain as originally filed. Applicants have not pointed to support in the specification as originally filed for support for this amendment. As such the changing of the isolation strain is considered to add new matter to the disclosure. Applicants previously asserted that the amendment is supported by the sequence listing as originally filed. This is not persuasive, the sequence listing is devoid of information (written description) regarding the strain from which the sequence was derived. At no point does it indicate that the sequence was derived from

Applicant is required to cancel the new matter in the reply to this Office action.



Claim Objections

5. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. in the instant case claim 5 depends from claim 3. Claim 3 is drawn to a specific DNA sequence and variants thereof whereas claim 5 is drawn to encoding a protein sequence (a recitation that is broader than claiming a specific DNA sequence) and variants thereof thus, the dependence of claim 5 from claim 3 is seen to broaden the scope of the claims.

Claim Rejections - 35 USC § 112

6. Claims 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants points to the originally filed claims, on page 2, lines 16-19 and page 7, lines 19-24. The claims are drawn to DNA encoding a heterologous fusion DNA encoding F1 and V proteins, wherein the V antigen is from other species of *Yersinia* having a V antigen which is homologous to *Y. pestis* V antigen. The original claims only describe DNA wherein the F1 and V are both from *Y. pestis*. Page 2, lines 16-19 describe the V- antigen and this passage does not

provide written description support for the now claimed DNA or support that applicants had conceived at the time of invention, such a hybrid DNA. Page 7 , lines 19-24 describe a vaccine comprising *antibodies* to the F1-V protein of *Y. pestis* in combination with a V-antigen of *Y. enterocoliticia* and *Y pseudotuberculosis* in a pharmaceutically acceptable, again this passage does not remotely support the now claimed F1-V DNA where in the V antigen is from a different species, this passage is drawn to a vaccine combination of antibodies with heterologous V antigens. Again this passage does not provide written description to support that applicants, had at the time of filing conceived of the now claimed invention. Applicants are required to cancel the new matter in response to this office action.

7. The rejection of claim 11 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn over claim 15 only, the rejection over claim 11 is maintained for reasons made of record.

Applicants' arguments have been carefully considered with respect to claim 11, but are not persuasive. Applicants argue given the commercial availability of the starting products E.coli and plasmid from Novagen, the disclosure of SEQ ID NO:1 and high skill in the art, one skilled in the art would be able to reproduce the pF1-V plasmid. This is not persuasive, the correct strain for the isolation of the V antigen DNA was not originally disclosed (see new matter rejection above). moreover, there is no evidence of record, that the originally filed strain would exactly reproduce the pF1-V plasmid as asserted. In view of the new matter rejection above, the only means to overcome this rejection is a deposit for patent purposes. Even if one were to

overcome the new matter rejection, applicants have not demonstrated that the Antigua strain of *Y. pestis* is commercially available and thus the assertion that the skilled artisan with all the starting materials and method steps would lead to the claimed pF1-V plasmid is not persuasive. The rejection over claim 11 is maintained for reasons made of record.

8. The rejection of claims 1-10, 12-17, 30 and new claims 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained for reasons made of record for claims 1-10, 12-17, 30 in Paper No 8, mailed 11-10-97.

Applicants arguments have been carefully considered but are not persuasive. Applicants argue that it would not require undue experimentation to produce the variants but still encode the desired antigen. This is not persuasive, the rejected claims have no protein sequence and therefore no codon redundancy can envisioned. Neither part of the protein, F1 or V has any specific protein structure. One skilled in the art can not envision or make changes due to codon redundancy when there is no recited protein structure in the claims. Moreover, the term "encoding" in the claim encompasses these variants. Applicants argues that the protective epitopes of these protein are known in the art (see page 9, lines 10-11 wherein the reference of Motin et al 1994 is cited). This is not persuasive because the teaching of Motin et al can not be properly evaluated since the reference is not of record. The passage does not indicate that protective epitopes are taught by Motin et al but merely that "..the invention also include fragments of F1 or V containing protective epitopes [Motin *et al.* (1994) *Infect Immun.* **62**:4192-4201] and thus it is not clear what is taught by Motin. It is well established in the art that

changes in primary sequence can substantially affect the folding of a protein and presentation of "protective" epitopes. Applicants also allege that when applicants sequenced the F1-V fusion DNA fragment of the present invention, two nucleotides were different between the F1-V fusion fragment and the previously published sequence of the V antigen indicating that changes can occur without affecting the ability of the DNA to encode F1-V fusion protein. This is not persuasive because there is no specific protein structure in the rejected claims at all. Thus, one skilled in the art would not be able to access F1-V ability to protect or relatedness to another sequence. Applicants are not enabled for infinite variants of a protein with no structure. Moreover, the recitation of "F1" or "V" does not connotate any sequence structure and thus applicants arguments are not commensurate in scope with the claims. In contrast to applicants assertions there are no physical or biological characteristics of the F1 or V antigen in the claims and the limitations and characterization of the F1-V individual protein of the specification are not read into the claims.

The rejection is maintained.

9. Claims 1-10, 12-17, and 30 and new claims 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons made of record in Paper No. 8, mailed 11-10-97. This was a written description rejection. The rejection was not addressed and is therefore maintained. Applicants response of 2-25-99 did not address this issue of paragraph 8. Lack of written description is not to be confused with lack of enablement, applicant has argued enablement not written description. Applicant is reminded

that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

The rejection is maintained. No variants, synthetic or natural or *Yersinia* DNA homologues are described in the specification.

10. Claims 1-3 and 5-17, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/18231 (Titball et al.-31) and further in view of: WO 95/24475 (Titball et al.-'75); or Leary et al. Infection and Immunity 63(8): 2854-58 8/95, publicly available as of 7/25/97).

Applicants argue the references do not specifically teach the claimed DNA encoding a F1-V fusion protein antigen. This point is moot since the rejection was based under obvious in light of 103(a) and not anticipated under 102. Applicants argue that the references do not suggest the claimed DNA. This is not persuasive. *In re* Fine, 837 F.2d 1071, 1075, 5U.S.P.Q.2d 1959 (Fed. Cir. 1988) states that under section 103 a *prima facie* case of obviousness can be established by showing some objective teaching in the prior art **or** that knowledge generally available to one of ordinary skill in the art can lead the individual to combine the references. In the instant case the examiner has provided ample motivation to make a fusion protein

"..it would have been obvious to one of ordinary skill in the art to link the gene encoding the F1 protein as set forth by Titball et al. 31 to the gene encoding the V antigen as set forth by Leary et al since a DNA construct encoding the fusion protein would have been expected to provide a vaccine with higher efficacy than a DNA construct which only encodes for the V antigen (or F1 antigen). Furthermore, it would have been obvious for one of ordinary skill in the art to link the gene encoding the F1 protein to the gene encoding the V protein since the time and cost to

make a F1 antigen fused to the V antigen would have been expected to be less than making the antigens independently. "... it would have been obvious to one of ordinary skill in the art to link the gene encoding the F1 protein as set forth by Titball et al. 31 to the gene encoding the V antigen as set forth by Titball et al -75 since a DNA construct encoding the fusion protein would have been expected to provide a vaccine with higher efficacy than a DNA construct which only encodes for the V antigen (or F1 antigen). Furthermore, it would have been obvious for one of ordinary skill in the art to link the gene encoding the F1 protein to the V protein since the time and cost to make a F1 antigen fused to the V antigen would have been expected to be less than making the antigens independently. Applicants also argue that it is well known that the fusion of one protein to another may result in instability of the protein and cites E. Amann to support this assertion. This is not persuasive, the Amann reference has not been provided and the teachings relied upon can not be properly evaluated. In addition, the art teaches that both F1 and V produced as fusion proteins with heterologous proteins are stable. Thus, applicants argument regarding the stability of fusion proteins are not persuasive since the fusion proteins of F1 and V of the art were stable. Thus, the production of a fusion protein comprising "all of the F1 and V antigens" would be reasonably be expected to be stable, absent factual evidence to the contrary.

Applicants allegation of the fusion of the F1 antigen with a portion of the V antigen are also not persuasive since the claims are drawn to "all of" the F1 and V antigen and not portions thereof.

The rejection is maintained.

Status of Claims

11. All claims stand rejected.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Patricia A. Duffy, Ph.D.
January 31, 2000

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600